REMARKS/ARGUMENTS

This is in response to the Final Office Action dated October 16, 2003 rejecting original claims 1-36. Independent claims 1, 18 and 19 are amended, and claim 5 is canceled herein. Claims 1-4 and 6-36 are thus pending.

Rejection Under 35 U.S.C. 112

The Examiner rejects claims 1-36 under 35 USC 112, first paragraph, asserting there is no support in the specification for the phrase "pharmacologically acceptable lipophilic liquid vehicle with at least one membrane-forming lipid."

Applicants respectfully direct the Examiner to portions of the specification which clearly support this claim limitation. [See p. 27, lns. 16-23; p. 30, lns. 17-26.] Reconsideration and allowance of pending claims 1-4 and 6-36 is respectfully requested.

The Examiner further rejects claims 1-36 under 35 USC 112, second paragraph, asserting that it is unclear whether the membrane-forming lipid is the same as or different from the outer layer phospholipid. Independent claims 1, 18 and 19 are herein amended to further clarify the distinction between these claim limitations. Reconsideration and allowance of all pending claims is respectfully requested.

Rejection Under 35 U.S.C. 103:

Claims 1-8 and 12-17 are rejected under 35 U.S.C. 103(a) based on Haynes (US 4725442) by itself or in view of Burke (US 5552156).

Claims 9-11 and 18-36 are also rejected under 35 U.S.C. 103(a) based on Haynes or in combination with Burke, and further in view of WO 99/61001.

Independent claims 1, 18 and 19 as amended herein are directed to injectable pharmaceutical compositions that include an aqueous microdroplet suspension or carrier solution having a pH less than 6.5. As discussed in the specification, "the continuous aqueous phase of the microdroplet dispersion composition is preferably acidic, i.e., have a pH less than

7 in order to minimize hydrolysis of the α-hydroxy lactone ring of camptothecins mediated by hydroxyl species such as can occur in base catalyzed hydrolysis." [p. 24, lns. 7-13.] "Some advantages believed to be provided by the microdroplet composition include protection of the α-hydroxy lactone functional group from hydrolysis in aqueous media..." [p. 24, lns. 26-31.] These and other limitations recited in the pending claims are neither suggested nor disclosed in the references cited by the Examiner.

Haynes does not disclose camptothecins as acknowledged by the Examiner (p. 4) nor is any desired pH limitations associated therewith disclosed that would be directed to minimizing the hydrolysis of the α-hydroxy rings of camptothecins. Moreover, Burke does not disclose or suggest having an aqueous suspension or dispersion of microdroplets with a pH less than 6.5 as recited in the pending claims. Rather, as noted by the Examiner, Burke "discloses that the lipid encapsulation creates an internal environment with a low pH to prevent hydrolysis of camptothecin drugs." (p.4) "The pH of the internal environment of the liposomes or micelles may be reduced pH which prevents hydrolysis of those camptothecin drugs which have lower affinity for the liposome or micelle membrane." [Burke, Abstract; see also col. 21, lns. 22-26 - "Thus camptothecin drugs are stabilized in liposomes either by binding the liposome membrane or by locating in the compartment where the pH is lower than 6, preferably 5 or below."] The references in Burke to internal environments and compartments of the liposomes and micelle structures do not disclose or suggest acidic aqueous suspensions or dispersions of microdroplets as claimed by Applicants.

Reconsideration and allowance of pending claims 1, 18 and 19 including all claims dependent thereon is respectfully requested.

CONCLUSION

It is submitted that the present application is in form for allowance, and such action is respectfully requested. Should the Examiner have any questions, please contact the undersigned attorney.

The Commissioner is authorized to charge any additional fees which may be required, including petition fees and extension of time fees, to Deposit Account No. 23-2415 (Docket No. 12636-898).

Respectfully submitted,

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